Ethanol

CAS #64-17-5
Swiss CD-1 mice, at 0, 5, 10, and 15% in water
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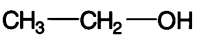

Ethanol (EtOH) was evaluated as a known positive in the RACB protocol using CD-1 mice (Morrissey et al., Fundam Appl Toxicol 13:747–777 [1989]). A dose-range-finding study provided data on water consumption, body weights, and clinical signs, which were used to select concentrations for the continuous cohabitation phase (Task 2) of 5, 10, and 15% weight per volume in distilled water. Water consumption was reduced at the middle and highest concentrations, by approximately 9 and 25%, respectively. Interestingly, body weights remained unchanged during the course of Task 2. These concentrations, consumption, and body weight data produced calculated consumption estimates of approximately 8.5, 16.0, and 20 g/kg/day.

While the mean number of litters per pair was unchanged by EtOH consumption, the number of live pups per litter was reduced by approximately 20% at the high dose. Viability, sex ratio, and pup body weight (absolute or adjusted for litter size) was unaffected by EtOH consumption. Study days on which the third, fourth, and five litters were delivered were 2 to 7 days later at the high dose compared to the controls.

It was concluded that EtOH was causing no significant reproductive toxicity during Task 2, so a Task 3 crossover was not performed, and second-generation effects (Task 4) were evaluated in the control and high dose groups only.

The last litter from the control and 15% EtOH groups was nursed by the dam until weaning at postnatal day 21, then provided with the same dosed water as their parents. While the viability of the F_1 pups was unaffected by parental EtOH exposure, body weight was reduced by approximately 25% at weaning. At the time of mating (approximately postnatal day 74), male and female body weights in the 15% EtOH group were 13 and 7% less than their respective controls.

EtOH did not affect the proportion of F_1 pairs mating or delivering live young, and the number and viability of those young were also unchanged. The weight of the F_2 pups, adjusted for litter size, was reduced in the EtOH-exposed group by approximately 7%.

After the F_2 pups were evaluated, all animals were killed, and the F_1 parents were necropsied. For the EtOH-exposed group, male terminal body weight was 10% less than controls. Absolute testis weight was unchanged, while adjusted weights of liver and kidneys were increased in the EtOH-exposed mice by 11 and 12%, respectively. Epididymal sperm motility was reduced from a control value of 80% motile, to 55% in the EtOH-consuming group; there were no changes in epididymal sperm density or morphologic abnormalities. Female mice consuming 15% EtOH weighed 8% less than controls at sacrifice, while adjusted liver weight and kidney weight was increased by 13 and 11%, respectively.

In summary, ethanol, at concentrations sufficient to affect water consumption more than body weight, had only modest reproductive effects (reduced sperm motility and increased time between litters) in Swiss CD-1 mice. These effects mirror those found in literature reports.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB86144979/AS**
Chemical: **Ethanol**
CAS#: **64-17-5**
Mode of exposure: **Water**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	5%	10%	15%
General toxicity	Male, female	Male, female	Male, female
Body weight	—, —	—, —	—, —
Kidney weight[a]	•	•	•
Liver weight[a]	•	•	•
Mortality	—, —	—, —	—, —
Feed consumption	•	•	•
Water consumption	—, —	↓, ↓	↓, ↓
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
$\bar{x}$ litters/pair	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	↓, —
Cumulative days to litter	—	—	↑
Absolute testis, epididymis weight[a]	•	•	•
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	•
Epidid. sperm parameters (#, motility, morphology)	•	•	•
Estrous cycle length	•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	•	•

F_1 generation — Dose concentration →	5%	10%	15%
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	•	•	↓, ↓
Mortality	•	•	—, —
Adult body weight	•	•	↓, ↓
Kidney weight[a]	•	•	↑, ↑
Liver weight[a]	•	•	↑, ↑
Feed consumption	•	•	•
Water consumption	•	•	—, —
Clinical signs	•	•	—, —
Reproductive toxicity			
Fertility index	•	•	—
# live pups/litter; pup wt./litter	•	•	—, ↓
Absolute testis, epididymis weight[a]	•	•	—, —
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	—, —
Epidid. sperm parameters (#, motility, morphology)	•	•	—, ↓, —
Estrous cycle length	•	•	•

Summary information	
Affected sex?	**Unclear**
Study confounders:	**None**
F_1 more sensitive than F_0?	**Unclear**
Postnatal toxicity:	**Yes**

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); —, —, no change in males or females. [a]Adjusted for body weight.